

WHAT IS CLAIMED IS:

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1. A sustained release nail varnish composition comprising:
 - (a) a pharmaceutically effective agent;
 - (b) a humectant;
 - (c) water;
 - (d) less than about 7.5% (w/w) based on the total weight of the composition, of a polymeric film-forming agent;
 - (e) at least one additional excipient; and
 - (f) a solvent system including at least one volatile solvent.

2. The nail varnish of claim 1, wherein said pharmaceutically effective agent is selected from the group consisting of an antifungal agent, a keratolytic agent and mixtures thereof.

Sub B2 3. The nail varnish of claim 2, wherein said antifungal agent is selected from the group consisting of amphotericin B, butefanine, butoconazole, carbol-fuchsin, ciclopirox, clioquinol, clotrimazole, econazole, gentian violet, ketoconazole, miconazole, naftifine, nystatin, oxiconazole, sodium thiosulfate, terbinafine, terconazole, tolnaftate, undecylenic acid,

~~ically accepta~~

~~claim 3~~

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~~claim 2, wherein said~~
~~about 5% (w/w) base~~

Sub-B3

~~claim 2, wherein~~

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10. The nail varnish of claim 2, wherein said keratolytic agent is present in an amount of from about 0.05% to about 5% (w/w) based on the weight of the non-volatile components.

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11. A nail varnish of claim 2, wherein said pharmaceutically effective agent further comprises an antibacterial agent, an antiviral agent, an antipsoriatic agent or mixtures thereof.

12. A nail varnish of claim 11, wherein said antibacterial agent is selected from the group consisting of bacitracin, clindamycin, erythromycin, gentamicin, mupirocin, neomycin, tetracyclines, polymyxin B, benzalkonium chloride, boric acid, hexachlorophene, iodine, iodoquinol, mafanide, mercury ammoniated, metronidazole, nitrofurazone, selenium sulfide, silver

	1970	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031	2032	2033	2034	2035	2036	2037	2038	2039	2040	2041	2042	2043	2044	2045	2046	2047	2048	2049	2050	2051	2052	2053	2054	2055	2056	2057	2058	2059	2060	2061	2062	2063	2064	2065	2066	2067	2068	2069	2070	2071	2072	2073	2074	2075	2076	2077	2078	2079	2080	2081	2082	2083	2084	2085	2086	2087	2088	2089	2090	2091	2092	2093	2094	2095	2096	2097	2098	2099	2100	2101	2102	2103	2104	2105	2106	2107	2108	2109	2110	2111	2112	2113	2114	2115	2116	2117	2118	2119	2120	2121	2122	2123	2124	2125	2126	2127	2128	2129	2130	2131	2132	2133	2134	2135	2136	2137	2138	2139	2140	2141	2142	2143	2144	2145	2146	2147	2148	2149	2150	2151	2152	2153	2154	2155	2156	2157	2158	2159	2160	2161	2162	2163	2164	2165	2166	2167	2168	2169	2170	2171	2172	2173	2174	2175	2176	2177	2178	2179	2180	2181	2182	2183	2184	2185	2186	2187	2188	2189	2190	2191	2192	2193	2194	2195	2196	2197	2198	2199	2200	2201	2202	2203	2204	2205	2206	2207	2208	2209	2210	2211	2212	2213	2214	2215	2216	2217	2218	2219	2220	2221	2222	2223	2224	2225	2226	2227	2228	2229	2230	2231	2232	2233	2234	2235	2236	2237	2238	2239	2240	2241	2242	2243	2244	2245	2246	2247	2248	2249	2250	2251	2252	2253	2254	2255	2256	2257	2258	2259	2260	2261	2262	2263	2264	2265	2266	2267	2268	2269	2270	2271	2272	2273	2274	2275	2276	2277	2278	2279	2280	2281	2282	2283	2284	2285	2286	2287	2288	2289	2290	2291	2292	2293	2294	2295	2296	2297	2298	2299	2300	2301	2302	2303	2304	2305	2306	2307	2308	2309	2310	2311	2312	2313	2314	2315	2316	2317	2318	2319	2320	2321	2322	2323	2324	2325	2326	2327	2328	2329	2330	2331	2332	2333	2334	2335	2336	2337	2338	2339	2340	2341	2342	2343	2344	2345	2346	2347	2348	2349	2350	2351	2352	2353	2354	2355	2356	2357	2358	2359	2360	2361	2362	2363	2364	2365	2366	2367	2368	2369	2370	2371	2372	2373	2374	2375	2376	2377	2378	2379	2380	2381	2382	2383	2384	2385	2386	2387	2388	2389	2390	2391	2392	2393	2394	2395	2396	2397	2398	2399	2400	2401	2402	2403	2404	2405	2406	2407	2408	2409	2410	2411	2412	2413	2414	2415	2416	2417	2418	2419	2420	2421	2422	2
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sulfadiazine, salts thereof, derivatives thereof and mixtures thereof.

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A4 } 13. The nail varnish of claim 11, wherein said antibacterial agent is present in an amount of from about 0.01% to about 1% (w/w), relative to the total weight of the composition.

14. The nail varnish of claim 11, wherein said antibacterial agent is present in an amount of from about 0.05% to about 5% (w/w), based on the weight of the non-volatile components.

15. A nail varnish of claim 11, wherein said antiviral agent is selected from the group consisting of acyclovir, amantadine, cidofovir, famciclovir, foscarnet, ganciclovir, palivizumab, penciclovir, ribavirin, rimantadine, valcyclovir, salts thereof, derivatives thereof, and mixtures thereof.

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AS } 16. The nail varnish of claim 11, wherein said antiviral agent is present in an amount of from about 0.08% to about 0.8% (w/w), relative to the total weight of the composition.

17. The nail varnish of claim 11, wherein said antiviral agent is present in an amount of from about 0.8% to about 8% (w/w), based on the weight of the non-volatile components.

18. A nail varnish of claim 11, wherein said antipsoriatic agent is selected from the group consisting of alclometasone, amcinonide, betamethasone, clobetasol, clocortolone, desonide, desoximetasone, diflorasone, fluocinolone, ~~fluocinonide~~, flurandrenolide, halcinonide, hydrocortisone, mometasone, prednicarbate and triamcinolone, salts thereof, derivatives thereof, and mixtures thereof.

19. The nail varnish of claim 11, wherein said antipsoriatic agent is present in an amount of from about 0.02% to about 2% (w/w), relative to the total weight of the composition.

20. The nail varnish of claim 11, wherein said antipsoriatic agent is present in an amount of from about 0.1% to about 10% (w/w), based on the weight of the non-volatile components.

21. The nail varnish of claim 1, wherein said humectant is selected from the group consisting of glycerol, sorbitol and mixtures thereof.

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A7 → 22. The nail varnish of claim 1, wherein said humectant is present in an amount of from about 3% to about 15% (w/w), relative to the total weight of the composition.

23. The nail varnish of claim 1, wherein said humectant is present in an amount of from about 5% to about 35% (w/w), based on the weight of the non-volatile components.

24. The nail varnish of claim 1, wherein said water is present in an amount of less than about 5% (w/w), relative to the total weight of the composition.

25. The nail varnish of claim 1, wherein said water is present in an amount of from about 0.4% to about 25% (w/w), based on the weight of the non-volatile components.

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26. The nail varnish of claim 1, wherein said polymeric film-forming agent is selected from the group consisting of hydrophobic (water insoluble) polymers.

27. The nail varnish of claim 26, wherein said hydrophobic (water insoluble) polymer is selected from the group consisting of hydrophobic cellulose derivatives, hydrophobic methacrylic polymers, cellulose acetate phthalate, shellac, (derivatives thereof), and mixtures thereof. *remove parentheses*

28. The nail varnish of claim 27, wherein said hydrophobic cellulose derivative is selected from the group consisting of ethyl cellulose of any acceptable molecular weight. *112*

29. The nail varnish of claim 27, wherein said hydrophobic methacrylic polymer is selected from the group consisting of methacrylic acid copolymer type B (USP/NF), methacrylic acid copolymer type C (USP/NF), ammonio methacrylate copolymer type B (USP/NF) and ammonio methacrylate copolymer type A (USP/NF), derivatives thereof, and mixtures

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thereof.

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30. The nail varnish of claim 1, wherein said polymeric film-forming agent is present in an amount of from about 8% to about 35% (w/w), based on the weight of the non-volatile components.

31. The nail varnish of claim 1, wherein said polymeric film-forming agent is present in a weight ratio of polymer to antifungal agent from about 1:0.01 to about 1:0.3.

32. The nail varnish of claim 1, wherein said polymeric film-forming agent is present in a weight ratio of polymer to keratolytic agent from about 1:0.01 to about 1:1.

33. The nail varnish of claim 1, wherein said polymeric film-forming agent is present in a weight ratio of polymer to antibacterial agent from about 1:0.01 to about 1:0.3.

34. The nail varnish of claim 1, wherein said polymeric film-forming

agent is present in a weight ratio of polymer to antiviral agent from about 1:0.02 to about 1:0.2.

35. The nail varnish of claim 1, wherein said polymeric film-forming agent is present in a weight ratio of polymer to antipsoriatic agent from about 1:0.006 to about 1:0.15.

36. The nail varnish of claim 1, wherein said at least one additional excipient is selected from the group consisting of plasticizers.

37. The nail varnish of claim 36, wherein said plasticizer is selected from the group consisting of dibutyl sebacate, diethyl phthalate, lanolin alcohols, mineral oil, petrolatum, polyethylene glycol, propylene glycol, triacetin, triethyl citrate, and mixtures thereof.

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A9 } 38. The nail varnish of claim 36, wherein said plasticizer is present in an amount of from about 0.1% to about 2% (w/w), relative to the total weight of the composition.

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39. The nail varnish of claim 36, wherein said plasticizer is present in an amount of from about 0.5% to about 10% (w/w), based on the weight of the non-volatile components.

40. The nail varnish of claim 36, wherein said plasticizer is present in a weight ratio of plasticizer to polymer from about 0.04:1 to about 0.3:1.

41. The nail varnish of claim 1, wherein said volatile solvent is selected from the group consisting of an alcohol, a ketone, and mixtures thereof.

42. The nail varnish of claim 41, wherein said alcohol is selected from the group consisting of ethanol, isopropyl alcohol, methanol and mixtures thereof, and further wherein said ketone is acetone.

43. The nail varnish of claim 1, wherein said volatile solvent is a mixture of acetone and isopropyl alcohol.

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44. The nail varnish of claim 1, wherein said volatile solvent is

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present in an amount of from about 60% to about 90% (w/w), relative to the total weight of the composition.

45. The nail varnish of claim 43, wherein said acetone and said isopropyl alcohol are present in a volumetric ratio of acetone to isopropyl alcohol from about 1:4 to about 4:1.

46. The nail varnish of claim 1, wherein said solvent system further includes at least one non-volatile solvent selected from the group consisting of benzyl alcohol, benzyl benzoate, corn oil, cottonseed oil, ethyl oleate, glycerin, glycofural, isopropyl myristate, isopropyl palmitate, mineral oil, peanut oil, polyethylene glycol, propylene glycol, propylene carbonate, sesame oil, soybean oil, water, and mixtures thereof.

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47. A sustained release nail varnish composition comprising:

- (a) an antifungal agent;
- (b) a keratolytic agent;
- (c) a humectant;
- (d) water;

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- (e) a polymeric film-forming agent;
- (f) at least one additional excipient; and
- (g) a solvent system including at least one volatile solvent.

48. The nail varnish of claim 47, wherein said antifungal agent is selected from the group consisting of amphotericin B, butefanine, butoconazole, carbol-fuchsin, ciclopirox, clioquinol, clotrimazole, econazole, gentian violet, ketoconazole, miconazole, naftifine, nystatin, oxiconazole, sodium thiosulfate, terbinafine, terconazole, tolnaftate, undecylenic acid, therapeutically acceptable salts thereof, derivatives thereof and mixtures thereof.

49. The nail varnish of claim 48, wherein said antifungal agent is clotrimazole or miconazole nitrate.

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50. The nail varnish of claim 47, wherein said antifungal agent is present in an amount of less than about 1% (w/w), relative to the total weight of the composition.

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51. The nail varnish of claim 47, wherein said antifungal agent is present in an amount of less than about 5% (w/w) based on the weight of the non-volatile components.

52. The nail varnish of claim 47, wherein said keratolytic agent is selected from the group consisting of urea, sulfur, salicylic acid, podophyllum resin and mixtures thereof

53. The nail varnish of claim 47, wherein said keratolytic agent is urea.

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54. The nail varnish of claim 47, wherein said keratolytic agent is present in an amount of less than about 1% (w/w) relative to the total weight of the composition.

55. The nail varnish of claim 47, wherein said keratolytic agent is present in an amount of from about 0.05% to about 5% (w/w) based on the weight of the non-volatile components.

56. The nail varnish of claim 47, further comprising an antibacterial agent, an antiviral agent, an antipsoriatic agent or mixtures thereof.

57. The nail varnish of claim 56, wherein said antibacterial agent is selected from the group consisting of bacitracin, clindamycin, erythromycin, gentamicin, mupirocin, neomycin, tetracyclines, polymyxin B, benzalkonium chloride, boric acid, hexachlorophene, iodine, iodoquinol, mafenide, mercury ammoniated, metronidazole, nitrofurazone, selenium sulfide, silver sulfadiazine, salts thereof, derivatives thereof and mixtures thereof.

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A14 7 58. The nail varnish of claim 56, wherein said antibacterial agent is present in an amount of from about 0.01% to about 1% (w/w), relative to the total weight of the composition.

59. The nail varnish of claim 56, wherein said antibacterial agent is present in an amount of from about 0.05% to about 5% (w/w), based on the weight of the non-volatile components.

60. The nail varnish of claim 56, wherein said antiviral agent is

selected from the group consisting of acyclovir, amantadine, cidofovir, famciclovir, foscarnet, ganciclovir, palivizumab, penciclovir, ribavirin, rimantadine, valcyclovir, salts thereof, derivatives thereof, and mixtures thereof.

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A15 } 61. The nail varnish of claim 56, wherein said antiviral agent is present in an amount of from about 0.08% to about 0.8% (w/w), relative to the total weight of the composition.

62. The nail varnish of claim 56, wherein said antiviral agent is present in an amount of from about 0.8% to about 8% (w/w), based on the weight of the non-volatile components.

63. The nail varnish of claim 56, wherein said antipsoriatic agent is selected from the group consisting of alclometasone, amcinonide, betamethasone, clobetasol, clocortolone, desonide, desoximetasone, diflorasone, fluocinolone, fluocinonide, flurandrenolide, halcinonide, hydrocortisone, mometasone, prednicarbate and triamcinolone, salts thereof, derivatives thereof, and mixtures thereof.

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64. The nail varnish of claim 56, wherein said antipsoriatic agent is present in an amount of from about 0.02% to about 2% (w/w), relative to the total weight of the composition.

65. The nail varnish of claim 56, wherein said antipsoriatic agent is present in an amount of from about 0.1% to about 10% (w/w), based on the weight of the non-volatile components.

66. The nail varnish of claim 47, wherein said humectant is selected from the group consisting of glycerol, sorbitol and mixtures thereof.

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67. The nail varnish of claim 47, wherein said humectant is present in an amount of from about 3% to about 15% (w/w), relative to the total weight of the composition.

68. The nail varnish of claim 47, wherein said humectant is present in an amount of from about 5% to about 35% (w/w), based on the weight of the non-volatile components.

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69. The nail varnish of claim 47, wherein said water is present in an amount of less than about 5% (w/w), relative to the total weight of the composition.

70. The nail varnish of claim 47, wherein said water is present in an amount of from about 0.4% to about 25% (w/w), based on the weight of the non-volatile components.

71. The nail varnish of claim 47, wherein said polymeric film-forming agent is selected from the group consisting of hydrophobic (water insoluble) polymers.

72. The nail varnish of claim 71, wherein said hydrophobic (water insoluble) polymer is selected from the group consisting of hydrophobic cellulose derivatives, hydrophobic methacrylic polymers, cellulose acetate phthalate, shellac, derivatives thereof, and mixtures thereof.

73. The nail varnish of claim 72, wherein said hydrophobic cellulose

derivative is selected from the group consisting of ethyl cellulose of any acceptable molecular weight.

74. The nail varnish of claim 72, wherein said hydrophobic methacrylic polymer is selected from the group consisting of methacrylic acid copolymer type B (USP/NF), methacrylic acid copolymer type C (USP/NF), ammonio methacrylate copolymer type B (USP/NF) and ammonio methacrylate copolymer type A (USP/NF), derivatives thereof, and mixtures thereof.

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A18 } 75. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in an amount of less than about 7.5% (w/w), relative to the total weight of the composition.

76. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in an amount of from about 8% to about 35% (w/w), based on the weight of the non-volatile components.

77. The nail varnish of claim 47, wherein said polymeric

film-forming agent is present in a weight ratio of polymer to antifungal agent from about 1:0.01 to about 1:0.3.

78. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in a weight ratio of polymer to keratolytic agent from about 1:0.01 to about 1:1.

79. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in a weight ratio of polymer to antibacterial agent from about 1:0.01 to about 1:0.3.

80. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in a weight ratio of polymer to antiviral agent from about 1:0.02 to about 1:0.2.

81. The nail varnish of claim 47, wherein said polymeric film-forming agent is present in a weight ratio of polymer to antipsoriatic agent from about 1:0.006 to about 1:0.15.

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82. The nail varnish of claim 47, wherein said at least one additional excipient is selected from the group consisting of plasticizers.

83. The nail varnish of claim 82, wherein said plasticizer is selected from the group consisting of dibutyl sebacate, diethyl phthalate, lanolin alcohols, mineral oil, petrolatum, polyethylene glycol, propylene glycol, triacetin, triethyl citrate, and mixtures thereof.

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84. The nail varnish of claim 82, wherein said plasticizer is present in an amount of from about 0.1% to about 2% (w/w), relative to the total weight of the composition.

85. The nail varnish of claim 82, wherein said plasticizer is present in an amount of from about 0.5% to about 10% (w/w), based on the weight of the non-volatile components.

86. The nail varnish of claim 82, wherein said plasticizer is present in a weight ratio of plasticizer to polymer from about 0.04:1 to about 0.3:1.

87. The nail varnish of claim 47, wherein said volatile solvent is selected from the group consisting of an alcohol, a ketone, and mixtures thereof.

88. The nail varnish of claim 87, wherein said alcohol is selected from the group consisting of ethanol, isopropyl alcohol, methanol and mixtures thereof, and further wherein said ketone is acetone.

89. The nail varnish of claim 47, wherein said volatile solvent is a mixture of acetone and isopropyl alcohol.

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A20 } 90. The nail varnish of claim 47, wherein said volatile solvent is present in an amount of from about 60% to about 90% (w/w), relative to the total weight of the composition.

91. The nail varnish of claim 89, wherein said acetone and said isopropyl alcohol are present in a volumetric ratio of acetone to isopropyl alcohol from about 1:4 to about 4:1.

92. The nail varnish of claim 47, wherein said solvent system further includes at least one non-volatile solvent selected from the group consisting of benzyl alcohol, benzyl benzoate, corn oil, cottonseed oil, ethyl oleate, glycerin, glycofural, isopropyl myristate, isopropyl palmitate, mineral oil, peanut oil, polyethylene glycol, propylene glycol, propylene carbonate, sesame oil, soybean oil, water, and mixtures thereof.

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93. A method of preparing a sustained release varnish or spray formulation for treating the nail and surrounding tissues, comprising the steps of:

- (a) preparing a solution including at least one volatile solvent;
- (b) adding water to the solution prepared in (a);
- (c) dissolving the pharmaceutically effective agents, and excipients in the solution prepared in (b);
- (d) adding the humectant to the solution prepared in (c) when the formulation ingredients are completely dissolved; and
- (e) dissolving the polymeric film forming agents in the solution prepared in (d).

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